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POLLUTION-ASSOCIATED DISEASE CONDITIONS IN ESTUARINE/COASTAL FISH AND SHELLFISH: A STATUS REPORT AND PERSPECTIVE FOR THE 1990's

by

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FOREWORD

Twelve years ago, at a dimly-remembered Statutory Meeting of the Council, a paper was presented which attempted to summarize information on those diseases of marine fish and shellfish that seemed to have an association with estuarine/coastal pollution (Sindermann, 1977). The document (C.M.1977/E:14) presented data on disease conditions such as fin erosion, ulcers, lymphocystis, epidermal papillomas, and skeletal abnormalities in fish, as well as shell disease in crustaceans, emphasizing the circumstantial nature of much of the available evidence for a pollution:disease relationship.

Now, more than a decade later, it should be instructive to reexamine the premise that such a relationship may exist, in light of new information that has been published in the intervening years. Has the evidence become more definitive? Have statistical relationships been found? Have experimental studies helped to clarify results of field observations? With these and related questions in mind, the recent literature (since 1977) has been consulted and an attempt made to draw conclusions about findings to date--recognizing the possible transiency (or even the inaccuracy) of those conclusions.

This document is intended to be a discussion paper, recognizing that some investigators may have different interpretations of available data. It is offered with the hope that the question of pollution:disease relationships in the marine environment will continue to serve as an impetus for further research, especially within ICES member countries.

CONTENTS

ABSTRACT

This reexamination of associations of pollution and disease in estuarine/coastal marine fish and shellfish draws examples from five areas: (1) effects of pollutants on early life history stages; (2) effects of pollutants on the integument; (3) effects of pollutants on filtering/detoxifying systems; (4) effects of pollutants on cell and tissue metabolic pathways; and (5) effects of pollutants on immune responses. In each category, new information has been published which supports the hypothesis that certain disease conditions do have a relationship with habitat degradation.

The overriding influence of stress-inducing environmental conditions on disease is apparent in numerous studies. Physiological/biochemical pathways through which long-term stress may result in pathology have been elucidated for fish, and counterpart but analogous pathways have been suggested for molluscs and crustaceans. In fish, for example, fin erosion may be a consequence of continuous exposure of epithelium to toxic levels of chemicals, combined with hormonal/metabolic stress-related disturbances within the animal. With crustaceans, disturbed chitin synthesis in the presence of overwhelming populations of chitin-destroying microorganisms, may result in "shell disease." With bivalve molluscs, highly toxic chemicals such as tributyltin may interfere with normal calcification of the shell.

I. INTRODUCTION

Tentative indications of possible pollution-associated disease conditions in marine fish and shellfish began to appear in the scientific literature in the 1960's and early 1970's. As examples, Young (1964) reported a variety of gross pathological changes in fish taken near southern California's giant ocean outfalls; Young and Pearce (1975) found black gills and shell erosion in crustaceans from the New York Bight; and Mahoney et al. (1973) reported fin erosion in 22 species of fish from the New York Bight apex. During the same period, Rosenthal and his associates were beginning what was to become a long-term study of effects of pollutants on fish larvae (Kinne and Rosenthal, 1967; Rosenthal, 1971; Rosenthal and Stelzer, 1970; Rosenthal and Sperling, 1974; von Westernhagen et al., 1974).

Then in the late 1970's and throughout the 1980's, evidence for an association of numerous disease conditions in marine fish and shellfish with degraded habitats increased dramatically. Chronologically during that period, information accumulated about skeletal anomalies in fish (Valentine, 1975; Matsusato, 1978, 1986), ulcerations in cod (Christensen, 1981), epidermal papillomas in several species of flatfish (Stich et al., 1977; Dethlefsen, 1984; Dethlefsen and Lang, 1988), and liver tumors in fish (Murchelano and Wolke, 1985; Malins et al., 1984, 1988; Vethaak, 1987). Much of the available information about the effects of pollutants on marine animals was summarized admirably in a symposium "Toxic Chemicals and Aquatic Life: Research and Management" held in Seattle in 1986, with papers published in Volume 11 of Aquatic Toxicology (1988).

During the past decade, important new findings have added significantly to information about pollution and disease. Liver tumors and other lesions have been reported from flatfish sampled in grossly polluted estuarine locations in the United States and Europe. Genetic abnormalities in developing fish embryos and morphological abnormalities in larvae seem related, in several studies, to the extent of chemical pollution. Shell disease and associated "black gill disease" of crustaceans have been reported with higher prevalences and with greater severity in polluted habitats. This new information, augmenting results of earlier studies, adds substantially to the concept of an association of polluted habitats and fish and shellfish diseases, even though direct cause and effect relationships have not been demonstrated to the satisfaction of all observers.

The evidence, though substantial, for an association of polluted habitats and fish and shellfish diseases, should still be considered as largely "circumstantial" or "inferential," since direct cause and effect relationships have not been demonstrated to the satisfaction of all observers. As recently as 1985, a workshop convened by the Working Group on Pathology, of the International Council for the Exploration of the Sea (ICES), concluded that "An established link between diseases and pollution does not exist" and that "The most likely general effect of pollution is a non-specific lowering of resistance, resulting in appearance of variable disease signs rather than the specific induction of an identifiable syndrome" (Anonymous, 1985).

This assessment by the ICES Workshop participants seems unnecessarily pessimistic and negative, in view of the information summarized in this paper. Whereas it is certainly true that much of the evidence is circumstantial, and that more data are needed, it seems nonetheless that some measure of association between certain fish and shellfish diseases and pollution has been demonstrated. Studies employing a combination of field observations and experimental exposures to contaminants could do much to further reduce uncertainties. The body of evidence indicating a statistical relationship between degraded estuarine/coastal environments and certain disease conditions in fish and shellfish has grown to a point where other observers have concluded that a relationship does exist, and that what remains to be done is the acquisition of additional quantitative data and augmentation of supporting experimental information--especially that concerning the physiological/biochemical bases for observed pathology (Passino, 1984). Additionally, much more difficult studies of the effects of pollution-associated diseases on the abundance of resource species are still necessary. Results of analyses of disease-caused effects on survival are important to resource managers, even though such investigations constitute only a subset of the scientific examination of pollution/disease relationships.

The objectives of this paper are: (1) to examine the present understanding of specific disease conditions that may be associated with habitat degradation--including the ecological/physiological/biochemical mechanisms involved; (2) to assess the validity of associations that have been proposed; and (3) to suggest avenues of research that may prove to be productive in the 1990's.

II. STATUS REPORT ON DISEASE CONDITIONS ASSOCIATED WITH HABITAT DEGRADATION

Most of the disease conditions considered here are traceable to tissue damage and metabolic disturbances induced by toxic chemicals, or (in the case of infectious diseases) to increased infection pressure from expanded populations of facultative pathogens, combined with suppression of internal defense mechanisms of the stressed animals.

Searching for a structure that might lead to a sensible categorization of the various kinds of disease conditions to be discussed, one obvious approach would be to look at the animals at risk from the viewpoint of vulnerability to toxic levels of environmental contaminants, and to group the observed effects in this way. If this is done, areas of vulnerability that are apparent immediately include:

(A) Eggs and larvae;
(B) Integument;
(C) Filtering/detoxifying systems;
(D) Cell and tissue metabolic pathways; and
(E) Immune systems

The following sections are based on this structure--with the recognition that it is artificial, and that some disease conditions may be consequences of multiple effects of pollutants, through multiple pathways. Also, listing these five categories does not imply prioritization--since little agreement would be found; some authorities would consider effects on metabolic pathways as all important, while others would argue for primacy of effects on internal defenses. The categories are simply convenient and somewhat inclusive groupings--alternative ways of dissecting and discussing the pollution/disease relationship which has been explored in earlier papers (Sindermann, 1972, 1976, 1979, 1983, 1984, 1988a) (Fig. 1).

A. Effects of pollutants on early life history stages (eggs, embryos, and larvae)

Abundance of year classes of commercial fish and shellfish can be influenced, sometimes drastically, by environmental events before and after spawning, or during larval development. The possible role of contaminants in affecting survival is difficult to determine, except in experimental situations--but some important insights have been gained about abnormalities and mortalities in early life history stages (eggs, embryos, and larvae).

Some Effects of Toxic Levels of Pollutants

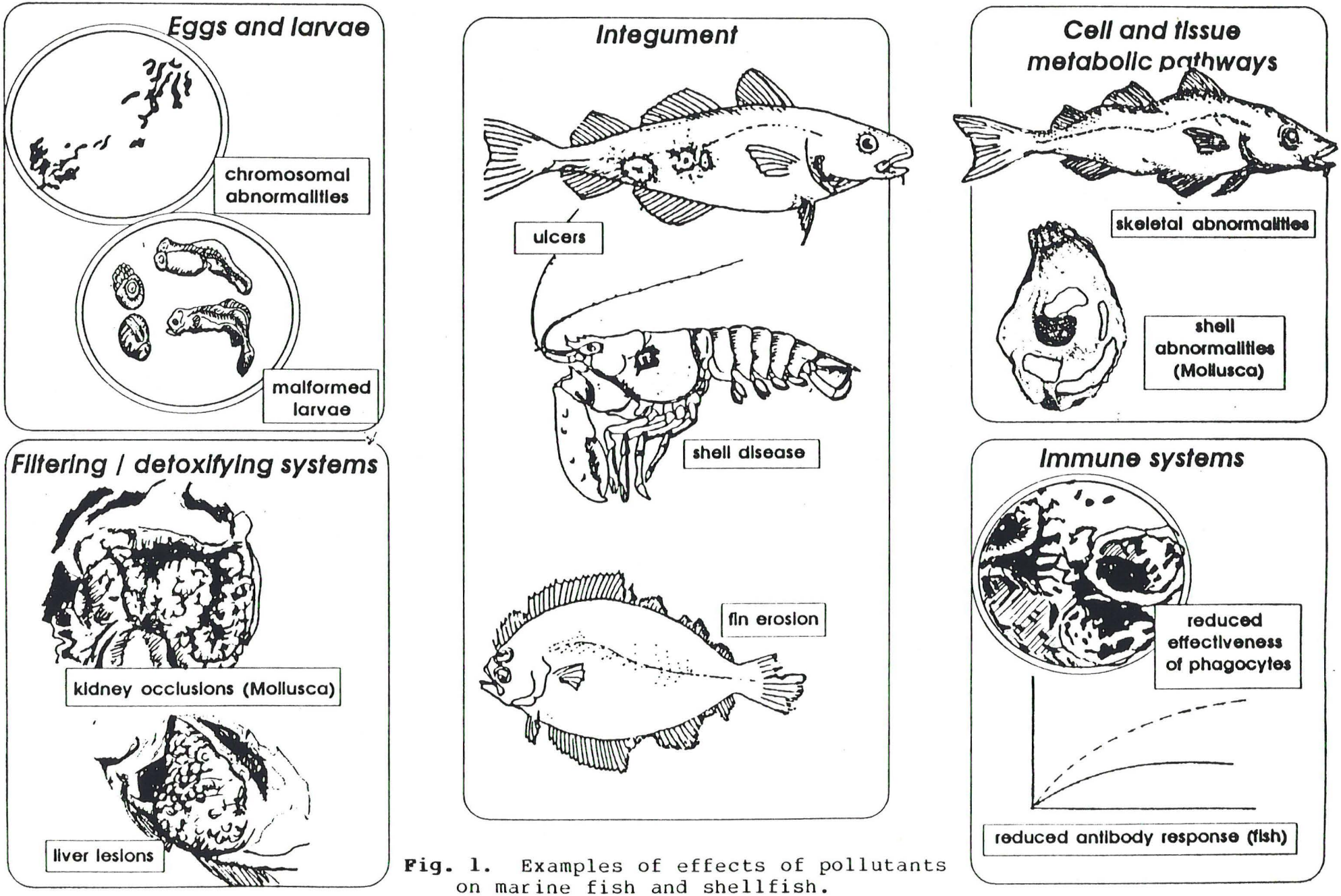

Fig. 1. Examples of effects of pollutants on marine fish and shellfish.

During the past two decades, two separate lines of investigation of pollutant effects on eggs and larvae have developed. The first is concerned with genetic and cytologic abnormalities in developing eggs; the other with abnormal larval development (with subsequent mortality). These investigations are obviously aspects of a common theme, and a wedding of disciplines is now occurring. Pioneering studies of cytotoxic and mutagenic effects of contaminants on marine fish eggs and larvae have been reported by Longwell (1976, 1977, 1978), Longwell and Hughes (1980), Longwell et al. (1983, 1884), Chang and Longwell (1984), and Hughes et al. (1986). Genetic disarray, represented morphologically by high prevalences of chromosomal anomalies in developing eggs and larvae, characterized samples from polluted waters. Examination of samples of developing embryos of mackerel from the New York Bight plankton disclosed cytological abnormalities (in the form of disruption of the mitotic apparatus) and chromosomal abnormalities (ranging from stickiness and chromosome bridges to complete pulverization). Statistical correlations of high prevalences of chromosomal anomalies with degree of environmental contamination provided evidence for possible impacts on estuarine/coastal populations.

Counterpart studies of gross effects of pollutants on developing fish larvae by Rosenthal and colleagues began in 1967 (Kinne and Rosenthal, 1967; Rosenthal and Stelzer, 1970; Rosenthal, 1971; von Westernhagen et al., 1974, 1975; Rosenthal and Alderdice, 1976; Hansen et al., 1985; Rosenthal et al., 1986)--and have been continued by Dethlefsen and von Westernhagen (Dethlefsen, 1980, 1984, 1985, 1988; Dethlefsen et al., 1987; von Westernhagen, 1988; von Westernhagen et al., 1981, 1987, 1988). Among the many significant findings reported in this excellent series of papers are these:

(1) Exposure of maturing females to low concentrations of contaminants--especially those which are bioaccumulated--can affect gonad tissue, with effects expressed in the next generation.

(2) Life cycle stages most vulnerable to contaminants are maturing females, early embryos, early hatched larvae, and larvae at transition from yolk sac to feeding.

(3) A wide range of morphological, behavioral, and physiological abnormalities in larvae result from exposure to contaminants, in rough proportion to the environmental level of the particular contaminant.

(4) Common morphological abnormalities include malformed lower jaw, eye deformities, anomalies in the vertebral column, and reduced size at hatching.

(5) Common physiological abnormalities include reduced heart rate, reduced swimming ability, disturbance in equilibrium, and reduced feeding.

(6) Early developmental stages showed the highest malformation rates.

Convergence of the two methodologies--cytogenetic and teratogenic--is now taking place, augmented by experimental studies of contaminant-exposed spawning fish, and by chemical analyses of tissue and environmental samples (see, for example, Dethlefsen et al., 1985, 1986; von Westernhagen et al., 1987, 1988). Chromosomal anomalies reported by Longwell and her associates suggest that at least some of the gross abnormalities in larvae observed by Rosenthal and his colleagues may have a genetic base, even though the kinds of derangements seen in the genetic material have not yet been correlated directly with the kinds of morphological and physiological disturbances seen. However, statistical associations of cytogenetic and teratogenic anomalies with degraded environments have been made. The unified approach, beginning with chromosomal damage in the ovaries of parent females and extending to gross larval abnormalities (Fig. 2), has great potential in bioindicator work, and has implications in population dynamics of estuarine/coastal species inhabiting polluted habitats (von Westernhagen et al., 1981, 1988; Sindermann, 1984).

Abnormalities induced by pollutants are of course only part of the spectrum of pollution effects; it is also important to examine mortalities that may result from exposure of pre-spawning females to contaminated habitats. Some evidence exists. Chlorinated hydrocarbons can contribute substantially to larval mortality, by accumulation in tissues and transfer to eggs from the parent females. In one specific example of larval mortality which seems related to increased environmental contamination, evidence was found that mortalities of larval winter flounder (Pseudopleuronectes americanus) in a Massachusetts estuary could be related to pesticide pollution (Smith, 1973). Adult females concentrated DDT, DDE, and heptachlor epoxide in their ovaries as spawning approached, and mortality of post yolk sac larvae approached 100%.

Other studies have provided evidence that high tissue concentration of chlorinated hydrocarbons in spawning adults can result in mortalities in developing eggs. Reproductive failure of a sea trout population in Texas was attributed to this phenomenon (Butler et al., 1972). The sea trout population inhabited an estuary that was contaminated heavily with DDT, and DDT concentration in the ovaries reached a peak of 8 ppm prior to spawning, compared to less than 0.5 ppm in sea trout from other less contaminated estuaries. Spawning seemed normal, but the eggs failed to develop.

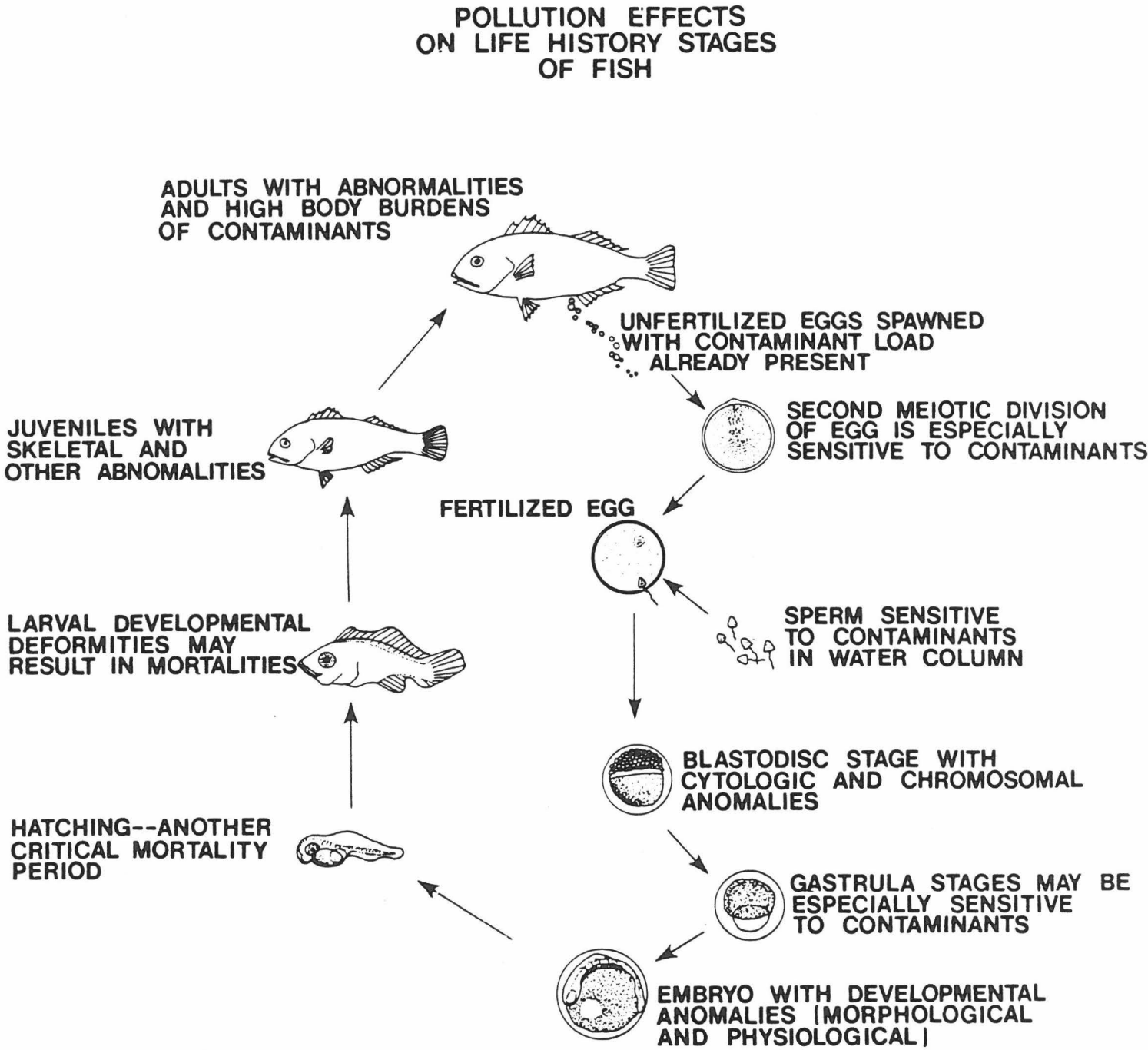

Fig. 2. Stages in the life history of fish where pollutant effects have been observed.

Several recent studies have indicated that high levels of PCBs in the gonads of spawning fish (Baltic flounder, Platichthys flesus; Baltic herring, Clupea harengus; striped bass, Morone saxatilis; and North Sea whiting, Merlangius merlangus) can result in low (< 50%) viable hatch of eggs, due to abnormal development and high embryo mortality (von Westernhagen et al., 1981, 1988; Hansen et al., 1985; Westin et al., 1985; Cameron et al., 1986).

Some experimental evidence indicates that specific pollutants may have effects on early life stages of fish. Studies by Weis et al. (1981) of killifish, Fundulus heteroclitus, disclosed that some females from unpolluted coastal areas produced eggs which were much more resistant to methyl mercury than eggs from other females (as measured by percentages of developmental anomalies which followed exposure). When a population from a heavily polluted coastal area was examined, a much higher percent of the females produced "resistant" eggs. However, subsequent studies have indicated that even though embryos from polluted areas were more resistant to methyl mercury toxicity, adults seemed less tolerant as determined by mortality and rate of fin regeneration (Weis et al., 1982). A recent review (Weis and Weis, 1987) summarized an excellent series of papers by the authors and their associates, published from 1974 to 1986, on experimental studies of pollutant-induced developmental abnormalities in killifish and other species. Included were considerations of teratogenic effects, optic and cardiac malformations, as well as skeletal defects.

Effects of contaminants also include hormonal imbalances, which may affect ovulation or spawning (Struhsaker, 1977; Wedemeyer et al., 1984). Additionally, hatchability of eggs and viability of larvae may be impaired, either by high tissue contaminant levels in the parent females, or by toxic levels of contaminants in the spawning environment (Ernst and Neff, 1977; Smith and Cameron, 1979; Hansen et al., 1985).

Of course the basic question that must be asked is "Can defective embryonic development and high embryo mortality due to pollution affect recruitment?" Some observations relative to this question have been proposed by von Westernhagen et al. (1988). According to their reasoning, total mortality during the embryonic stage of development of marine fish has been estimated to be high--95 to 99% for species such as Baltic cod and plaice, for example. At this mortality level, decreases in survival rates due to embryo abnormalities, at observed levels from 22 to 33%, would be too small to detect in unexploited populations, but in overexploited populations in which spawning stocks have been reduced severely, the added impact of abnormal embryonic development and high embryo mortality may result in reduced recruitment. The authors also point out that, for the North Sea,

the highest prevalences of embryo malformations occurred in highly polluted areas (off the mouths of the Rhine and Elbe rivers, and in the vicinity of the dumping zone for titanium dioxide wastes).

B. Effects of pollutants on the integument

The integument of aquatic animals is in continuous contact with environmental contaminants, so it is logical to assume that abnormalities could be consequences of such an intimate relationship. This assumption has been supported by results of studies of several disease conditions--particularly fin erosion and ulcerations in fish, and shell disease in crustaceans. Some of the clearest and statistically most defensible associations of pollution and disease are those signaled by the presence of integumentary lesions. Microbial pathogens are often, but not always, implicated.

1. Fin erosion. Probably the best known but least understood disease of fish from polluted waters is a nonspecific condition known as "fin rot" or "fin erosion," a syndrome which seems clearly associated with degraded estuarine or coastal environments--to the extent that it has been proposed as an index of pollutant-induced disease (O'Connor et al., 1987). Fin erosion has been reported from degraded estuarine/coastal areas in many parts of the world. It seems to occur in at least two types: one in bottom fish, where damage to fins seems site-specific and related to direct contact with contaminated sediments, and another in pelagic nearshore species, characterized by more generalized erosion, but with predominant involvement of the caudal fin.

Some species are either more resistant to fin erosion or are exposed differentially to toxic substances in water or sediments. A study by Wellings et al. (1976) in a heavily polluted arm of Puget Sound (the Duwamish River) in which over 6,000 fish of 29 species were examined, disclosed fin erosion only in starry flounder, Platichthys stellatus, and English sole, Parophrys vetulus. The authors briefly described observations of liver pathology in starry flounder from the area where fin erosion was common. Histopathology included increased fat deposition in hepatic cells, fibrosis, and vascular distension. Subsequent studies (Pierce et al., 1978), 1980) disclosed that all starry flounders from the Duwamish estuary with fin erosion also had severe liver lesions. A correlation of liver pathology and fin erosion was found also in Dover sole, Microstomus pacificus, from the California coast. Fin erosion, with prevalences up to 33%, was reported from over 30 species of marine fish in polluted sites in southern California (Cross, 1985; Malins et al., 1987). It seems quite likely that the "fin erosion" syndrome in fish may include participation of some or

all of the following: (1) chemical stressors, possibly acting on mucous and/or epithelial cells; (2) physiological responses of the fish to prolonged stress (particularly circulatory changes); (3) suppression of immune responses; (4) marginal dissolved oxygen concentrations, possibly enhanced by a sulfide-rich environment; and (5) secondary bacterial invasion in at least some instances.

2. Ulcerations. Vibrio and similar infections have been implicated in a number of reports of ulcerations in fish--in fact, next to fin erosion, ulcerations with bacterial etiology are probably the commonest abnormality in fish from polluted waters. Ulcers may be integumentary or penetrating; where bacterial isolations have been made from ulcerated tissue, Vibrio anguillarum has been by far the most predominant organism, with pseudomonads and aeromonads in lesser abundance. It seems to be a reasonable generalization that many of the infections that produce grossly visible ulcerations in fish are bacterial (although viruses and fungi have been implicated in a few instances), and are often due to pathogens of the genera Vibrio, Pseudomonas, or Aeromonas (Lamolet et al., 1976). Ulceration often begins with scale loss or formation of small papules, followed by sloughing of the skin, exposing the underlying muscles, which may also be destroyed. Bacterial ulcers may have rough or raised irregular margins, and will often be hemorrhagic. Ulcers may or may not be associated with fin erosion.

Epizootic ulcerative syndromes have been reported with increasing frequency in fish from many parts of the world, including the east coast of the United States (Sindermann, 1988b). Etiology is uncertain for many outbreaks, although viruses, bacteria, fungi, and other pathogens have been proposed in specific geographic locations. Environmental stress, often as a consequence of pollution, has also been implicated in at least some of the reported epizootics.

The ulcerative lesions do not constitute a single disease entity, since their characteristics may be quite different in different host species and areas (Fig. 3). Such lesions can be considered as generalized responses of fish to infection and/or abnormal environmental conditions. Types of ulcerations have been described, some with several developmental stages (Christensen, 1981), and mortalities have been observed in some outbreaks.

3. Shell disease in crustaceans. A disease condition in Crustacea commonly referred to as "shell disease" or "exoskeletal disease" or "shell erosion" has been associated with badly degraded estuarine and coastal waters. This abnormality can be considered in some ways as the invertebrate analogue of fin erosion in fish. Shell disease has been observed in many species

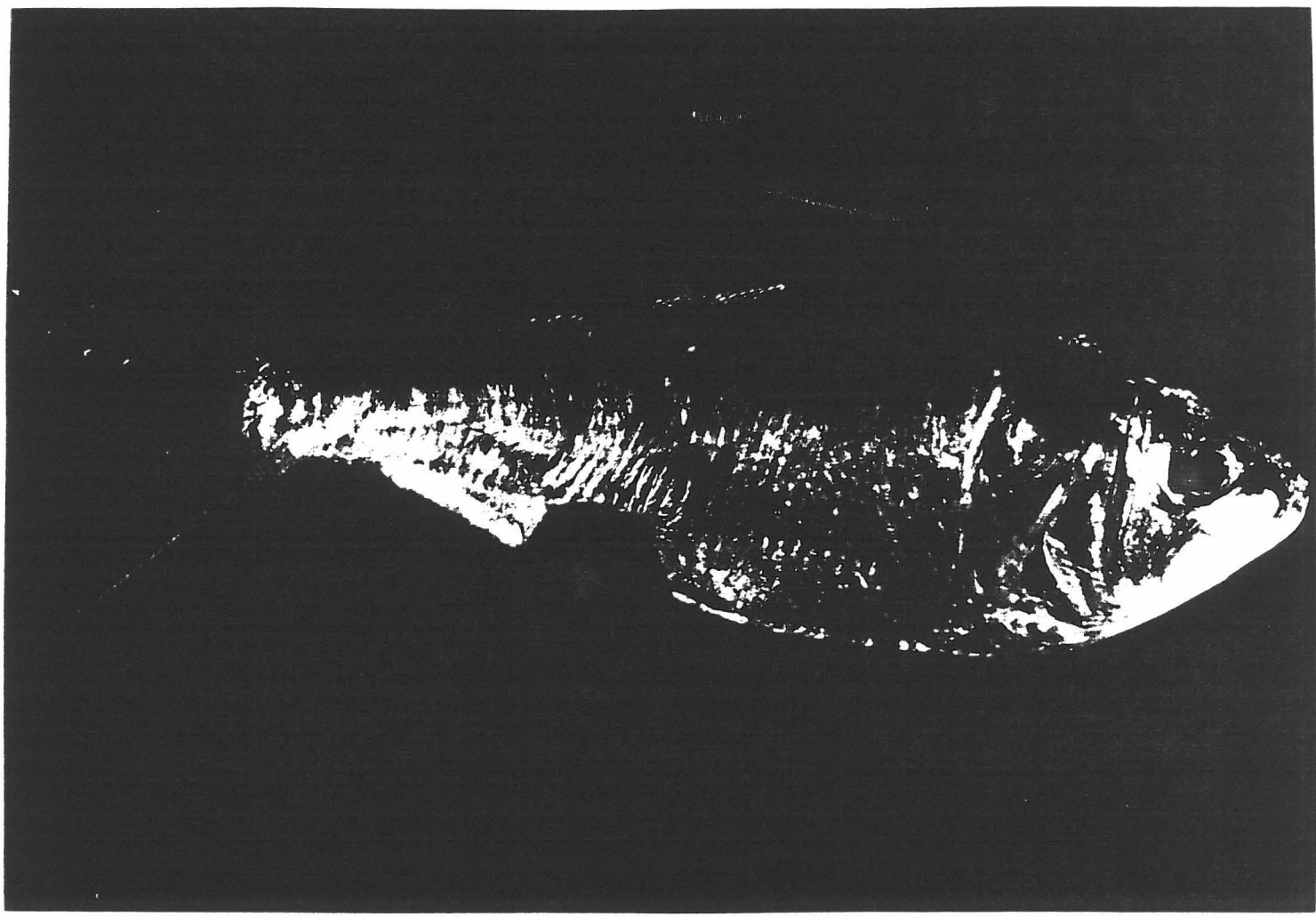

Fig. 3. Penetrating ulcer in the vent region of juvenile menhaden, Brevoortia tyrannus, from the Atlantic coast of United States. (Photograph provided by Dr. E. J. Noga.)

and under many conditions, both natural and artificial (Sindermann, 1989) (Fig. 4). Actual shell erosion seems to involve activity of chitinoclastic microorganisms, with subsequent secondary infection of underlying tissue by facultative pathogens. Initial preparation of the exoskeletal substrate by mechanical, chemical, or microbial action probably is significant; thus high bacterial populations and the presence of contaminant chemicals in polluted environments, as well as extensive detrital and epibiotic fouling of gills, could combine to make shell disease a common phenomenon and a significant mortality factor in crustaceans inhabiting degraded environments.

A recent study of shell disease in lobsters from Massachusetts waters disclosed highest prevalences in samples from the most polluted sites--particularly Boston Harbor and Buzzards Bay (Estrella, 1984). Mortalities were not observed, but population impacts were considered likely.

A detailed review of shell disease in crustaceans of commercial importance (Anonymous, 1989) resulted in the following general conclusions about relationships with pollution:

(1) "Shell disease may occur with higher prevalence and greater severity in polluted areas than in those not degraded by man's activities. The balance between metabolic processes associated with new shell formation, and infection by microbes capable of utilizing chitin, may be disturbed by environmental changes affecting normal shell formation or favoring the growth of chitin-utilizing microbes. Such disturbances may be consequences of pollution."

(2) "Evidence exists for an association of shell disease with habitat degradation. Prevalences have been found to be high in crustaceans from polluted sites; prevalences show trends similar to those of the black gill syndrome, which also has a statistical association with extent of pollution. Experimental exposures of crustaceans to contaminated sediments, heavy metals, biocides, petroleum, and petroleum derivatives can result in the appearance of the black gill syndrome, often accompanied by shell disease."

The physiology of crustaceans--especially that related to hormonal control of molting, has been elucidated by many studies during the past half-century. The role of pollutants in altering metabolic pathways involved is of course an area of concern. As an example, abnormal production of the steroid-molting hormones may inhibit cuticular synthesis, whereas hormonal insufficiency may delay or prevent molting, thereby affecting growth and survival. These metabolic anomalies may enhance effects of shell

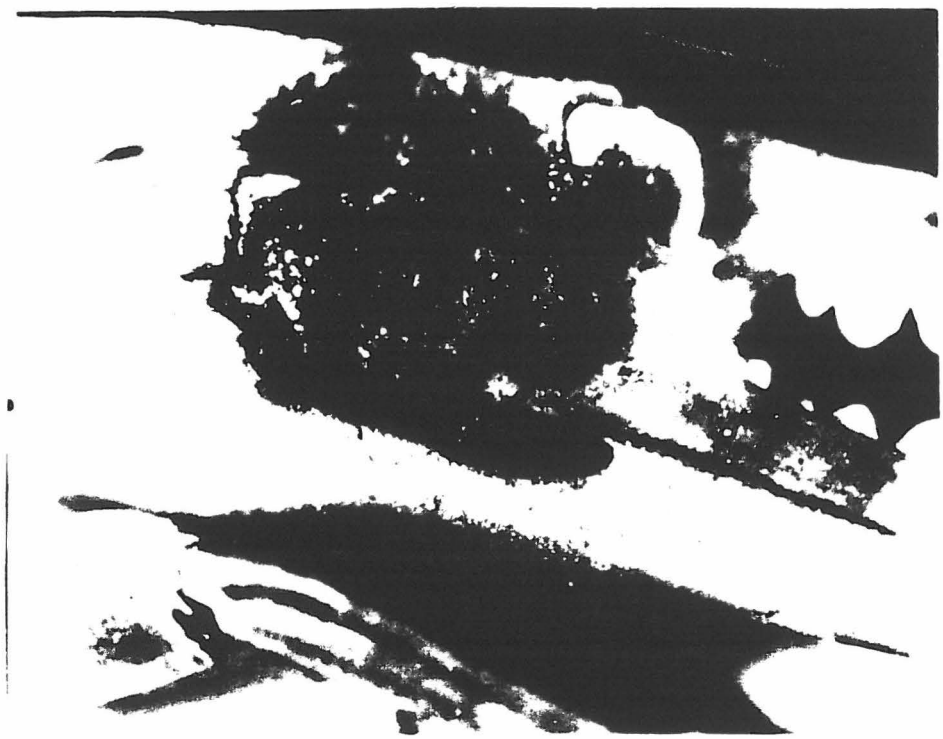

Fig. 4. Gross signs of shell disease in the claw of a blue crab, Callinectes sapidus. (Photograph supplied by Dr. R. M. Overstreet.)

disease, especially when accompanied by diminution of other cellular and humoral mechanisms of internal defense. The significance of a prophenoloxidase-activating system in crustacean responses to infection has been pointed out in a series of papers by Söderhäll (1982, 1983, 1986) and associates (1982, 1983, 1984, 1985, 1986), and the functioning of this system in the presence of pollutants can be important to host survival.

The appearance of shell erosion may therefore be the consequence of a disturbed balance between processes of chitin maintenance and repair and the activities of chitinoclastic microorganisms--this disturbance created by either natural or man-made environmental changes. Critical to an understanding of the relationship are environmental, genetic, and immunological factors which may either promote repair or, conversely, enhance exoskeletal degradation. Also essential to full understanding of the shell disease syndrome are further experimental studies, particularly those concerned with identification of specific microorganisms capable of pathogenesis, experimental manipulation of predisposing environmental variables, and the immunologic responses of hosts to cuticular disruption.

C. Effects of pollutants on filtering/detoxifying systems

Chemical examinations of fish and shellfish from grossly contaminated habitats frequently disclose high levels of heavy metals, chlorinated hydrocarbons, and polycyclic aromatic hydrocarbons in critical detoxifying sites (livers of fish, hepatopancreas of crustaceans). Pathological changes have also been seen in filtering organs such as the gills of fish and the kidneys of bivalve molluscs. Several disease conditions in such sites have been studied, and relationships with polluted habitats noted.

1. Liver tumors. Probably the best evidence for a relationship of tumors and coastal/estuarine pollution can be found in several studies of hepatomas (liver tumors) in fish. Smith et al. (1979) found that 25% of the livers of Atlantic tomcod, Microgadus tomcod, from the polluted Hudson River estuary contained neoplastic nodules and hepatomas (hepatocellular carcinomas), with highest prevalences in older fish. The authors suggested a possible association of hepatomas with elevated PCB levels in the Hudson River and in the livers of some specimens (Klauda et al., 1981). Other circumstantial evidence for a possible association of PCB contamination and hepatomas was reported from the North Pacific. A 32% prevalence of hepatomas was found in English sole, Parophrys vetulus, from the polluted

Duwamish River near Seattle, Washington--a river known to contain high levels of PCBs and other hydrocarbons (Malins et al., 1983).

The association of progressively severe liver pathology and several types of hepatic neoplasms with badly degraded estuarine/coastal waters is becoming more and more evident. Several new reports demonstrate this relationship. Winter flounder (Pseudopleuronectes americanus) from several degraded areas on the U.S. east coast (New Haven Harbor, upper Narragansett Bay, Boston Harbor) had prevalences of 3.4 to 7.5% tumors classified as hepatocarcinomas or cholangiocarcinomas (Murchelano and Wolke, 1985) (Fig. 5), while English sole (Parophrys vetulus) and rock sole (Lepidopsetta bilineata) from several sites on the northwest coast of United States (Commencement Bay, Eliot Bay, Everett Harbor, and Mukilteo Harbor) were found to have up to 16% hepatic neoplasms (Malins et al., 1984, 1988). The latter study included a detailed analysis of contaminants in tissues and sediments. Positive correlations were obtained between neoplasm prevalence in bottom-dwelling fish and levels of "certain individual groups of sediment-associated chemicals" (aromatic hydrocarbons, chlorinated hydrocarbons, and heavy metals), but a clear cause and effect relationship was not claimed by the authors. Limitations stated included present inability to identify all sediment-associated contaminants and uncertainty about the synergistic/antagonistic interactions among classes of chemicals.

Liver lesions described as tumors have been reported recently from flounder (Platichthys flesus) and dab (Limanda limanda) from Dutch coastal waters (Vethaak, 1987). Prevalences of gross lesions in fish older than three or four years were locally as high as 40%, and were higher in samples from polluted areas than those from less polluted waters.

What seems to be emerging from a number of studies of different species in different estuaries, is a sequence of histopathological changes in livers, beginning with fatty deposits and pre-neoplastic changes in liver parenchyma cells (Pierce et al., 1978; Köhler and Hölzel, 1980; Bucke and Feist, 1984; Kranz and Peters, 1985). The progression of pathological changes also seems roughly correlated with the extent of estuarine degradation and the length of residence of fish in the estuary. Also, high prevalences of macrophage aggregates (proposed pollution indicators) have been seen in histological material from polluted waters.

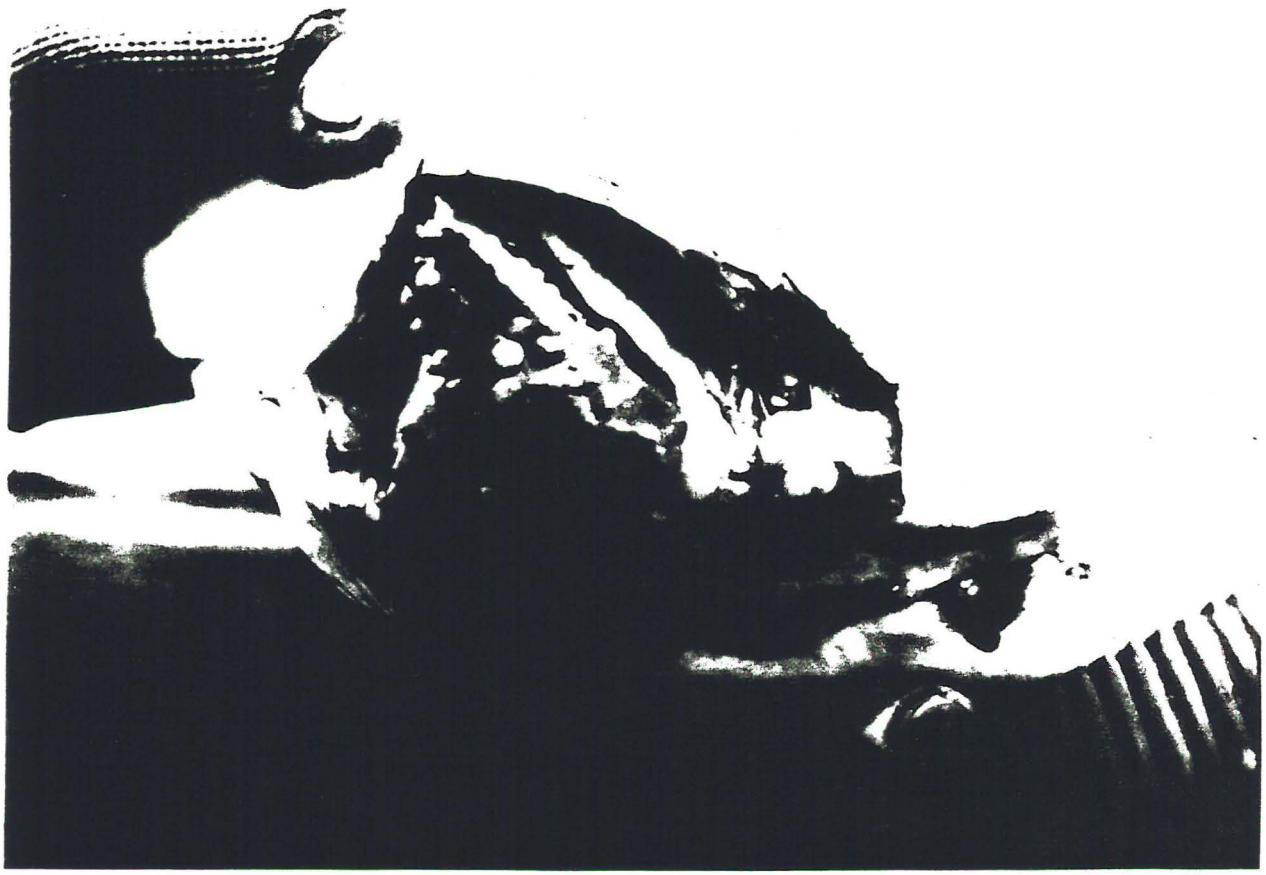

Fig. 5. Gross lesions in liver of winter flounder, Pseudopleuronectes americanus. (Photograph supplied by Dr. R. A. Murchelano.)

In addition to field observations and subsequent correlations of liver tumors and pollution, there is some experimental evidence for induction of liver neoplasms in marine/euryhaline fish by known carcinogens of higher vertebrates (summarized by Ishikawa and Takayama, 1979; Hendricks, 1982; Kimura and Ando, 1986; and Overstreet, 1988). The euryhaline Japanese medaka, Oryzias latipes, has been used in several studies, and is sensitive to carcinogens (methylazoxymethanol acetate and diethylnitrosamine). Liver and other tumors developed after brief exposure of early life history stages (Ishikawa et al., 1975; Aoki and Matsudaira, 1981; Kimura et al., 1984, 1986). Another euryhaline species, the sheepshead minnow, Cyprinodon variegatus, also developed hepatic and other neoplasms after exposure to methylazoxymethanol acetate and diethylnitrosamine (Hawkins et al., 1985a, b, 1988; Couch and Courtney, 1985). Additionally, the euryhaline species, Rivulus marmoratus, developed liver tumors after exposure to diethylnitrosamine (Koenig and Chasar, 1984).

2. Kidney concretions in molluscs. Information about excretory system concretions of calcium phosphate in bivalves is of recent origin (Doyle et al., 1978; Gold et al., 1982). Clams (Mercenaria mercenaria) and scallops (Argopecten irradians) from the U.S. east coast develop such concretions, which may occlude the entire kidney, and a relationship with polluted or abnormal environments has been proposed, based on the successful experimental induction of the deposits in the wedge shell, Donax trunculus (Mauri and Orlando, 1982), and on the finding that concretions in clams from polluted sites were more numerous and larger than those in clams from reference sites.

These kidney concretions are apparently distinct from the renal plugs described earlier as part of a stress syndrome in clams (Mercenaria mercenaria) from hydrocarbon-polluted sites in Narragansett Bay (Jeffries, 1972). That condition was characterized by a black tar-like mass which collected in the renal sac in quantities that appeared to plug the tubules and to interfere with kidney function. Masses of black hemocytes were also seen in mantle and kidney tissues.

D. Effects of pollutants on cell and tissue metabolic pathways

This category of effects has a significant degree of overlap with the previous one on filtration/detoxification systems--but is concerned more with consequences of the presence of abnormal levels of chemicals to the biochemistry of cells and tissues--as reflected by such abnormalities as some of the skeletal deformities in fish or anomalies in shell deposition in molluscs, in the presence of high environmental levels of contaminants such as tributyltin. Such abnormalities occur when the filtration/detoxification systems fail to cope with the influx of particular

toxic chemicals--which may then spill over into general circulation and affect cellular metabolic pathways. Examples that can illustrate some gross effects are skeletal deformities in fish and shell abnormalities in bivalve molluscs.

1. **Skeletal deformities in fish.** Skeletal anomalies, particularly those of the spinal column, are commonly observed in fish and are the subject of an extensive literature. Such anomalies may be genetic, resulting from mutations or recombinations, epigenetic, acquired during embryonic development; or postembryonic, acquired during larval or postlarval development (Hickey, 1972). Evidence exists for a hereditary basis for some skeletal anomalies, but other evidence points to effects of environmental factors such as temperature, salinity, dissolved oxygen, radiation, dietary deficiencies, and toxic chemicals. Pollutants may act as "developmental toxicants," exerting their effects, particularly on embryos, through several metabolic pathways (Weis and Weis, 1987).

Malformations of embryos of Baltic herring (Clupea harengus membras) were found to be abundant and in great variety following exposure to crude oil and chemical dispersants (Linden, 1976). In a recent study of pelagic fish embryos from the North Sea, malformations were found with high frequency in several species (dab, Limanda limanda; flounder, Platichthys flesus; whiting, Merlangius merlangus; cod, Gadus morhua; and plaice, Pleuronectes platessa) taken in regions with known high contamination levels (Dethlefsen et al., 1986).

Several reports from Japan refer to high and increasing occurrences of skeletal anomalies in fish. Komada (1974) and Ueki and Sugiyama (1976) observed increasing numbers of malformed sweetfish or ayu, Plecoglossus altivelis, in rivers and culture farms. Skeletal abnormalities in mullet and eight other species from the Inland Sea of Japan were reported by Matsusato (1973). In a recent study, Matsusato (pers. commun., 1983) found increasing prevalences of two skeletal syndromes (bent spines and fused vertebrae) as he ascended an estuary (Kurose River) contaminated upstream with chlorinated hydrocarbons and organophosphates. His sample consisted of 28,000 fish of 68 species. Matsusato (1986) also summarized all reports of skeletal anomalies--especially spinal fractures--in wild fish of Japan, concluding that occurrences were nationwide, with highest prevalences in agricultural rather than industrial areas, possibly because of pesticide contamination of habitats.

Deformed fin rays and associated skeletal abnormalities have been observed repeatedly in winter flounders from the highly polluted waters of the New York Bight (Ziskowski et al., 1980), and a summarization of observations on skeletal anomalies and related developmental defects has been published (Sindermann et al., 1978). Related anomalies, in the form of disruption in normal scale patterns and even scale reversal, have been noted in samples from polluted waters of Biscayne Bay, Florida (W. Kandrashoff, unpubl. data). The presence and frequency of such scale pattern anomalies may, along with skeletal abnormalities, be good indicators of the extent of environmental degradation (Sindermann et al., 1980).

Experimental evidence exists for induction of skeletal abnormalities by exposure to environmental contaminants. Couch et al. (1977) reported severe scoliosis and associated pathology in the sheepshead minnow, Cyprinodon variegatus, exposed to the organochloride pesticide Kepone. The authors concluded that scoliosis was a secondary effect of Kepone toxicity, with the nervous system or calcium metabolism as the primary target. Couch et al. (1979) also found that trifluralin (Treflan) induced extensive osseous hyperplasia in vertebrae of sheepshead minnows when life history stages from zygote to 28-day juveniles were exposed to 25-50 ppb trifluralin. Centra of vertebrae, thickened by active osteoblasts and fibroblasts, increased in size up to 10-30 times their normal dimensions--a striking sublethal effect. Bengtsson and Larsson (1986) found increased incidence of vertebral defects in sculpin exposed to effluents containing heavy metals. Disturbed plasma ionic balance in deformed fish was observed, and decreased collagen synthesis was proposed as a possible explanation for the abnormalities (Bengtsson et al., 1988).

2. **Shell abnormalities in bivalve molluscs.** Pacific oysters, Crassostrea gigas, were introduced to the coast of France in the late 1960's and to the British east coast in the early 1970's. By the mid-1970's, a serious problem with reduced growth and malformed shells was apparent, and the cause was found to be organotin compounds used on boats in antifouling paints. Abnormally thickened shells in exposed populations of oysters had an open laminar structure, a formation described as "chambering," sometimes with a proteinaceous gel secreted between the layers. In one French study, such abnormalities in shell calcification reached 90% during 1980-1982 in the Bay of Arcachon, but fell to 40% in 1983-1985, after a ban on use of tributyltin in antifouling paint was imposed (Alzieu et al., 1982, 1986). The severity of the deformations and the tissue levels of tin also decreased during the same period, confirming the chemical etiology of the condition. The extreme sensitivity of oysters to

tributyltin is apparent from findings that concentrations of only 50 ngl^{-1} could induce shell malformations (Alzieu et al., 1986). In a British study, C. gigas spat cultured in the presence of low environmentally feasible levels of the contaminant grew less well than controls, and developed pronounced thickening and chambering of the upper shell valve (Waldock and Thain, 1983). Higher levels of exposure resulted in increasing percentages of mortalities. [It seems relevant to note here that in other studies, experimental exposure of crabs, Uca pugilator, to tributyltin retarded limb regeneration, delayed ecdysis, and produced deformities in regenerated appendages (Weis et al., 1987). Decreased survival and reduced growth of lobster and crab larvae were also observed following exposure to tributyltin (Laughlin and French, 1980).]

E. Effects of pollutants on disease resistance

The immune system of fish has been investigated for more than half a century, and some measure of understanding has been achieved. The internal defenses of shellfish have been studied sporadically for a comparable period, with less definitive results, although new insights have been acquired recently. Pollutant effects on immunity in fish may take the form of immunosuppression, whereas in invertebrates effects on phagocytic activity have been demonstrated. Wherever examined, though, whether in fish or shellfish, the important role of pollutants as environmental stressors has been recognized.

1. Immunosuppresion in fish. Suppression of immune responses by toxicants such as heavy metals and pesticides has been demonstrated repeatedly in mammals, and some evidence indicates similar effects in fish (see, for example, Robohm and Nitkowski, 1974 and Stevens, 1977). The story of immunosuppression is not simple, however. Robohm et al. (1979) found that, for some species, such as the summer flounder, Paralichthys dentatus, antibody titers against bacteria common in the environment were higher and existed for a greater diversity of bacteria in fish from polluted waters than in those from an unpolluted reference site--the New York Bight versus Great Bay in southern New Jersey. Additionally, selection of high antibody responders among flatfish from the highly polluted New York Bight was reported recently by Robohm and Sparrow (1981). When tested experimentally against a battery of unrelated bacteria, fish taken from polluted waters were found to have higher antibody titers than those from unpolluted waters. This seems to be an example of compensatory population response, in which any reduction in internal defenses (immunosuppression in particular) in individual fish from degraded habitats could be offset by the development of a higher population level of immune competence as a result of selection.

Suppression of components of the cellular immune system of fish has been indicated in recent studies of several marine species from the highly polluted Elizabeth River, Virginia (Weeks and Warinner, 1984, 1987; Weeks et al., 1986). Using water from the river in experimental systems and fish kidney macrophages, the authors were able to demonstrate reduced phagocytosis and chemotactic activity, and an increase in the number of melanin granules in macrophages from Elizabeth River fish. The observed changes in immunological status were proposed as valuable in fish health monitoring in degraded habitats.

2. **Increased susceptibility to disease in shellfish.** Among the invertebrates, direct and indirect evidence for reduction of disease resistance caused by contaminant exposure exists, but is not abundant. A mechanism for increased susceptibility of clams to bacterial infection was proposed by Anderson et al. (1981) based on chronic (18 week) exposure to benzo[a]pyrene, pentachlorophenol, and hexachlorobenzene. Most of the exposed clams showed significantly impaired ability to clear injected bacteria (Flavobacterium sp.)--implying that resistance to bacterial invasion was decreased by exposure to xenobiotics. The deficiency in bacterial clearance was directly proportional to tissue levels of the chemicals used (some clams with high tissue burdens were totally unable to clear bacteria). Bacterial clearance may result from activity of cellular and humoral factors, and a number of these have been demonstrated in hard clams. Phagocytic activity (which was reduced after exposure to pollutants) was reported by Fries and Tripp (1980) as was the presence of bacterial agglutinins and lysins (Arimoto and Tripp, 1977; Anderson et al., 1981). Pollutant exposure has thus far been demonstrated to affect phagocytosis in hard clams and mussels (McCormick-Ray, 1987), but effects on humoral factors have not been reported.

Pollutants may affect cellular defenses of molluscs in a positive way as well. Phagocytic activity of oyster hemocytes has been reported to be enhanced by exposure to heavy metals (Cheng and Sullivan, 1984). In studies of mussels exposed to graded doses of copper ions, a dramatic increase in circulating granulocytes was seen, as was an increase in hemolymph lysozyme, total protein, and proteolytic activity (Pickwell and Steinert, 1984). Binding and sequestering of excess copper was a later phenomenon.

Some investigators have suggested that chronic pollution may place a stress on the animal which could be manifested in increased parasitism. Thus, Yevich and Barszcz (1983) noted that mussels, Mytilus edulis, from the northeast coast of the United States were more extensively and intensively parasitized (three to five species of unidentified parasites) than those from other areas. The authors pointed out that the increased parasitism

occurred in waters near great human population density and industrial activity. In a related study of the effects of chronic exposure to various crude oils on pond-held oysters, Barszcz et al. (1978) found a similar increase in prevalence and intensity of parasites--with the conclusion that resistance to infection is reduced in polluted environments, increasing susceptibility to opportunistic parasites.

VI. CONCLUSIONS

Based on the recent published information examined in this report, and recognizing the need for greater depth in many of the investigations, it is possible to propose a number of general conclusions:

- Disease is a significant limiting factor in estuarine/coastal populations of fish and shellfish; its effects may be enhanced by stresses resulting from abnormal environmental conditions--including (but not limited to) increases in population abundance of facultative pathogens, and toxic chemical concentrations which may affect metabolism.

- The critical role of environmental stressors, particularly toxic pollutants, in disease is becoming more and more obvious, and the pathways leading to pathology are receiving more attention too. Most of the disease conditions considered in this paper are indicators of stress. In fish, fin erosion, ulcerations, and decreased resistance to facultative pathogens are the indicators. In crustaceans, shell disease and black gills are signs; and in bivalve molluscs, poor growth and condition, mantle recession, and kidney concretions may give clues. This list of stress-induced abnormalities, which are all consequences of disturbed metabolism, may be augmented by other conditions--such as liver neoplasia in fish and shell abnormalities in bivalves--that seem related more directly to the effects of toxic levels of contaminants in the immediate environment, but are of course still indicators of disturbed metabolism.

- During the past decade, important new findings have added significantly to information about pollution and disease. Among them are these:

(1) Liver tumors and other lesions have been reported from flatfish sampled in grossly polluted estuarine locations in the United States and in Europe.

(2) Genetic abnormalities in developing fish embryos and morphological abnormalities in larvae seem related, in several studies, to the extent of chemical pollution.

(3) Shell disease and associated "black gill disease" of crustaceans have been reported with higher prevalences and with greater severity in polluted habitats.

- Because complex mixtures of chemical contaminants occur in badly degraded waters, specific pathologies in fish and shellfish cannot often be associated with specific contaminants in a cause and effect relationship. This is, however, feasible in experimental populations, and disease conditions such as fin erosion in fish and shell disease in crustaceans have been induced by laboratory exposures to contaminants. The problem has been stated precisely by Dethlefsen (1988):

  > "Given the present knowledge of ecosystems interactions it is unrealistic to expect that marine or aquatic science will be able in the near future to produce results that unequivocally document a connection between specific dysfunctions and specific pollutants. Such causal relationships can be demonstrated only for substances that are tested under controlled laboratory conditions. Whenever this proof has been required or expected for a complex ecosystem, the results have always been debated in the scientific community and therefore have been of no use in a pollution management context."

- It should be reemphasized, however, that extreme caution must be exercised in associating pollutants with disease conditions in fish and shellfish--a point made in great detail by Overstreet (1988). Many factors other than pollutants may be involved in producing lethal or sublethal effects; among them would be oxygen depletion, abnormal salinities or temperatures, or toxins from dinoflagellate blooms. Additionally, fish and shellfish species vary greatly in responses to abnormal environmental factors (including anthropogenic chemicals), and specific life stages may be remarkably different in susceptibility to variations in any single factor.

- In examining the available evidence for an association of certain disease conditions and habitat degradation, it is important to keep the quality and quantity of available data in mind. It is easy to err on the side of extremism--finding relationships lurking in even moderately disturbed environments; it is equally easy to err on the side of conservatism, discounting all observations as coincidental or circumstantial, and therefore irrelevant. Examples of suggested associations and correlations of pollution and disease, presented in section II of this paper, represent accumulations of data assembled by a number of observers. No studies, with the possible exception of those of fin erosion in the New York Bight apex and those of liver tumors in Puget Sound, have had the necessary broad multidisciplinary base to be described as "definitive" (although these two approach that level). The point to be emphasized here is that some correlations of disease prevalence and pollution have been made, but direct specific cause and effect relationships have not been established, except in experimental studies.

Despite obvious increases in public concern about effects of pollution on inhabitants of estuarine/coastal waters, attempts to slow the rate of environmental degradation will undoubtedly be part of a long-term process, since human populations living in the vicinity of coastal areas continue to expand. It is logical, therefore, to assume that pollution-associated disease problems in fish and shellfish will not disappear; at best they may be lessened slightly during the 1990's if efforts are made to reduce anthropogenic impacts in the most severely polluted areas. Pollution-associated disease conditions have often been recognized and studied in the worst estuarine/coastal environments that humans have created--places like the New York Bight apex, the mouths of the Elbe and Rhine rivers, the Duwamish River in Puget Sound, Tokyo Harbor, the Houston ship canal, to mention only a few. Decreases in contamination of these areas should at some point be reflected in reduction in prevalence and severity of stress-related disease conditions such as fin erosion, ulcerations, liver tumors, and shell disease.

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